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09/628,472	07/31/2000	Paul K. Wolber	10003511-1	5543

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	11

DATE MAILED: 04/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/628,472	Applicant(s) WOLBER ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FINAL ACTION

1. This action is in response to papers filed 8 February 2002 in Paper No. 7 in which claims 1, 5, 8 14 and 15 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 5 dated 3 October 2001 under 35 U.S.C. 112, second paragraph § a. and c. -g. are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

Currently claims 1-15 are under prosecution.

Requirement to Comply with Nucleic Acid Sequence Rules

2. Applicant's submission of Substitute Sequence listing in paper and computer-readable format in Paper No. 8 is acknowledged.

Specification

3. Applicant's submission of a Substitute Specification in Paper No. 9 is acknowledged.

Claim Objections

4. The previous Claim Objections are withdrawn in view of the amendments submitted in Paper No. 7.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

b. Claims 1-4, 14 and 15 are indefinite in Claim 1 for the recitation "subjecting said template array.....to primer extension reaction conditions under conditions sufficient to produce said mixture of nucleic acids" because it is unclear whether the recitation is a method step of primer extension. It is suggested that Claim 1 be amended to recite positive and active method steps to clearly define the invention e.g. delete "conditions under conditions sufficient".

Response to Arguments

7. Applicant argues that when read in light of the specification, the recitation "subjecting said template array.....to primer extension reaction conditions under conditions sufficient to produce said mixture of nucleic acids" is completely clear and not indefinite. The argument has been considered but is not found persuasive because whether the recitation is a method step of primer extension in which primer extension occurs or whether the recitation is merely a recitation of subjecting the template to conditions under which primer extension could occur. The claim does not recite a method step of primer extension, it merely recites subjecting the template to "conditions sufficient". Therefore, it is unclear whether primer extension occurs. The specification, page 10 lines 25-page 13, line 14 (page numbers of the original specification) describe various primer extension conditions. The specification does not that subjecting a template to primer extension conditions always results in primer extension. Therefore, read in light of the specification, Claim 1 is indefinite because it is unclear whether a step of primer extension is being claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, 10-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Cantor et al. (U.S. Patent No. 5,795,714, issued 18 August 1998).

Regarding Claim 1, Cantor et al. disclose a method for producing a mixture of nucleic acids comprising: providing an array of distinct single-stranded probe nucleic acids, contacting said array with nucleic acids complementary to said constant domain under hybridization conditions whereby a template array of overhang comprising duplex nucleic acids is produced, wherein each overhang comprising duplex of said array comprises a double-stranded region and a single-stranded variable region overhang; subjecting said template array to primer extension to produce a mixture of nucleic acids (Column 13, line 41-Column 14, line 22).

Regarding Claim 2, Cantor et al. disclose the method wherein said mixture of nucleic acids is a mixture of deoxyribo-oligonculeotides i.e. DNA (Column 6, lines 43-47).

Regarding Claim 3, Cantor et al. disclose the method wherein said constant domain comprises a linker domain (Column 15, lines 21-28).

Regarding Claim 4, Cantor et al. disclose the method wherein said step (c) comprise in vitro transcription i.e. enzymatic extension of the nucleic acids using the probe as a template (Column 14, lines 16-19).

Regarding Claim 10, Cantor et al. disclose a method of making a population of target nucleic acid molecules from an initial mRNA sample comprising: generating a mixture of nucleic acids according to the method of Claim 1 (Column 4, lines 48-61); employing said

mixture as primers in a target generation step in which target nucleic acids are produced i.e. to create duplicate arrays (Column 4, lines 48-50) wherein the nucleic acids are RNAs (Column 6, lines 43-47).

Regarding Claim 11, Cantor et al. disclose the method wherein the target generation step comprises template driven primer extension (Column 4, lines 57-58).

Regarding Claim 12, Cantor et al. disclose the method wherein said target generation step produces labeled target nucleic acids (Column 9, lines 28-50).

Regarding Claim 14, Cantor et al. disclose the method of Claim 1 wherein the nucleic acids are labeled (Column 9, lines 1-27).

Response to Arguments

10. Applicant argues that Cantor produces a plurality of different nucleic acids attached to a surface instead of a heterogeneous mixture as claimed. The argument has been considered but is not found persuasive because Cantor discloses a method comprising the claimed method steps (Column 13, line 41-Column 14, line 22). It is unclear to the examiner how the "plurality of different nucleic acids" produced by primer extension in Cantor differ from the claimed mixture of nucleic acid produced using the same method steps. While Cantor teaches the additional method step of immobilizing, the open claim language "comprising" of the instant invention encompasses the additional step of immobilizing the plurality of different nucleic acids taught by Cantor.

Applicant further argues that while Cantor does employ primer extension, he never mixes the products to produce a mixture. The argument has been considered but is not found persuasive because, it is noted that the features upon which applicant relies (i.e., mixing the products to produce a mixture) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims are drawn to methods of producing a mixture of nucleic acids comprising subjecting a template array to primer extension conditions. As Applicant notes (page 6, last full paragraph), Cantor subjects a template array to primer extension conditions to produce a plurality of different (i.e. mixture) nucleic acids. Cantor then immobilizes the mixture to produce a mixture of immobilized nucleic acids. However, as stated above, the open claim language "comprising" encompasses the additional step of immobilization in the method of Cantor.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 5-9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al. (U.S. Patent No. 5,795,714, issued 18 August 1998) and Dattagupta et al. (U.S. Patent No. 4,734,363, issued 29 March 1988).

Regarding Claim 5, Cantor et al. teach a method for producing a mixture of a plurality of distinct deoxyribo-oligonucleotides of differing sequence wherein each oligonucleotide comprises a different variable region (Column 7, lines 35-65) comprising: providing an array of a plurality of surface immobilized single stranded probes wherein each probe on the array is described by the formula L-R+F-cV-5' wherein L is an optional linker domain (Column 15, lines 21-28); R+F is the constant domain and cV –5' is the random domain (Column 14, lines 8-16); contacting the array under hybridizing conditions with a population of nucleic acids complementary to the constant domain whereby an overhang duplex nucleic acid is produced; and subjecting the duplex nucleic acids to primer extension whereby a mixture of oligonucleotides of differing sequence is produced (Column 14, lines 16-27). Cantor et al. do not each the constant domain comprises a recognition domain and a functional domain. Dattagupta et al. teach a similar method for producing a mixture of distinct deoxyribo-oligonucleotide wherein the a plurality of single-stranded probes having the formula: A-B-C-5'

wherein is A recognition domain, B is functional domain and C is a variable domain; contacting the probes with nucleic acids having the formula A' B'; and subjecting the overhang duplex to primer extension to thereby produce a plurality of nucleic acids (Column 4, lines 27-53) wherein the functional + recognition domains function to recognize the target sequence and transcription initiation site (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the constant domain of Cantor et al. with the functional + recognition domains as taught by Dattagupta et al. to thereby provide target recognition and transcription initiation for the expected benefit of efficient and specific transcription as taught by Dattagupta et al. (Column 3, lines 33-40).

Regarding Claim 6, Cantor et al. teach the linker domain of 0 bases (Column 15, lines 21-27).

Regarding Claim 7, Dattagupta et al. teach the similar method wherein the functional domain is an RNA polymerase promoter domain (Column 5, lines 22-27).

Regarding Claim 8, Cantor et al. teach the method wherein the recognition domain is recognized by a restriction endonuclease (Column 15, lines 29-39).

Regarding Claim 9, Cantor et al. teach the method wherein said step (c) comprise in vitro transcription i.e. enzymatic extension of the nucleic acids using the probe as a template (Column 14, lines 16-19).

Regarding Claim 13, Cantor et al. teach a method of generating a set of target nucleic acids according to the method of Claim 10; contacting said set of nucleic acids with nucleic acids under hybridizing condition; and detecting the presence of target nucleic acids hybridized to nucleic acids i.e. the generated nucleic acids are free in solution and hybridized to other nucleic acids for detecting the nucleic acids (Column 4, lines 48-65). Cantor et al. do not teach the nucleic acids in solution are contacted with an array of probes. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the hybridization of Cantor et al. by hybridizing the generated nucleic acids to probes

on an array to thereby detect the generated sequences using positional screening for the expected benefit of rapidly and accurately the sequence of the nucleic acid generated as taught by Cantor et al. (Column 4, lines 11-15).

Regarding Claim 15, Cantor et al. teach the method of Claim 1 for producing a mixture of nucleic acids comprising: providing an array of distinct single-stranded probe nucleic acids, contacting said array with nucleic acids complementary to said constant domain under hybridization conditions whereby a template array of overhang comprising duplex nucleic acids is produced, wherein each overhang comprising duplex of said array comprises a double-stranded region and a single-stranded variable region overhang; subjecting said template array to primer extension to produce a mixture of nucleic acids (Column 13, line 41-Column 14, line 22) but they do not specifically teach said method further comprises washing unbound target away from the surface of the array. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the teaching of Cantor et al. by further washing unbound target from the surface of the array for the obvious benefit of eliminating non-specific sequences and reducing background hybridizations.

Response to Arguments

13. Applicant argues that Cantor does not teach producing a mixture of nucleic acids and Dattagupta fails to make up the deficiency of Cantor and as such the combined teaching of Cantor and Dattagupta fail to teach a method of producing a mixture. The arguments have been considered but are not found persuasive because as stated above in ¶ 10, Cantor teaches the method as claimed. The claims are drawn to methods of producing a mixture of nucleic acids comprising subjecting a template array to primer extension conditions. As Applicant notes (page 6, last full paragraph), Cantor subjects a template array to primer extension conditions to produce a plurality of different (i.e. mixture) nucleic acids. Cantor then immobilizes the mixture to produce a mixture of immobilized nucleic acids. However, as stated above, the open claim language "comprising" encompasses the additional step of immobilization in the method of Cantor.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
April 18, 2002

W. Gary Jones
Supervisory Patent Examiner
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